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CERTIFICATE OF TRANSLATION

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that I know well both the French and English languages;

that I read the specification, claims and abstract as filed in U.S. Provisional Patent Application No. 60/428,702, filed November 25, 2002; and

that the attached English translation is a true and accurate translation to the best of my knowledge and belief.

Paris, May 24, 2004

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AN ANALYTE-TAKING DEVICE

The present invention relates to analyte-taking devices, and more particularly but not exclusively to those for use in taking at least one analyte, e.g. an ion, an organic compound, or biological material from the surface of a tissue, e.g. a skin.

The invention seeks specifically to facilitate analyte-taking for the purpose of establishing a diagnosis or an evaluation of the state of an individual, and in particular of the state of that individual's skin.

US patent No. 3 958 571 discloses an applicator comprising a tube containing a liquid and having an applicator element at one end of the tube. Such an applicator is designed to apply medication such as a solution of iodine.

There exists a need for an analyte-taking tool that is easy to transport, and that is capable of being made at low cost so as to be suitable for single use.

In one of its aspects, the invention provides an analyte-taking device comprising:

· a tube provided at one end with an analyte-taking element;

· a plug of a liquid or a powder inside the tube; and

· at least one liquid contained in an inside space of the tube separated from the analyte-taking element at least by the plug of liquid or powder, the plug being arranged, in use, to be evacuated together with the liquid towards the analyte-taking element, the liquid possibly being:

· an analyte-taking liquid suitable for facilitating the taking of at least one analyte by the analyte-taking element, for example suitable for impregnating the analyte-taking element so as to make it suitable for use on a tissue of an individual for taking at least one analyte present at the surface of said

tissue and enabling said analyte to be analyzed subsequently; or

- a reagent suitable for producing an observable reaction in the presence of a determined analyte picked up by the analyte-taking element.

The invention makes it possible to provide means that are relatively simple and inexpensive for taking an analyte from the skin, for example, in order to perform a diagnosis or an evaluation.

In addition, using the invention, it is easy to ensure that the quantity of analyte-taking liquid or of reagent contained in the analyte-taking device is kept down to the minimum quantity that is just sufficient by suitably selecting the dimensions of the tube.

The term "analyte" is used to designate a compound that is present at the surface of the skin, the mucous membranes, or the hair, or present in a body fluid such as urine, tears, saliva, or sweat, and that is capable of reacting with a specific reagent in order to be detected or quantified or in order to measure its activity. The analyte may be present in a cutaneous secretion such as sebum. The analyte may comprise microorganisms and/or substances associated therewith, whether dead or alive, and in particular it may comprise dead skin cells. The analyte may also comprise lipids or enzymes present, for example, on the skin or on the mucous membranes. By way of example, the analyte may form part of the group constituted by ions, in particular carbonate ions, bicarbonate ions, calcium ions, chlorine ions, potassium ions, and metal cations such as Cu^{2+}, Zn^{+}, Fe^{2+}, or Fe^{3+}, for example. The analyte may also form part of the group constituted by organic compounds, in particular free amino acids, peptides, proteins, or hormones.

The analyte may also comprise pollution residues, for example residues of arsenic, lead, mercury, iodine, or radioactive cesium.

The term "analyte-taking liquid" is used to designate any liquid enabling the analyte to be picked up, for example by dissolving it, fixing it, or transforming it. The analyte-taking liquid may be selected, for example, from the group constituted by: water; an aqueous solution; a water-alcohol solution; an oil solution; an oil; an organic solvent; chloroform; ethyl acetate; alcohols; chlorine-containing solvents; acetone; short esters; mixtures of water and methanol; and mixtures of chloroform and ethanol, this list not being limiting. It may also include an elutant and/or a fixer.

The term "reagent" is used to designate any compound, optionally in solution, that is suitable for reacting with a determined analyte in order to reveal its presence, or to quantify its concentration or its activity. By way of example, a reagent may change color or become bleached when coming into contact with a specific analyte. The reagent may be in the form of a powder, in the form of a gel, a hydrogel, a paste, or a liquid, amongst others.

When the device includes a reagent in the tube, the analyte-taking device may be pre-impregnated with an analyte-taking liquid, where appropriate.

The analyte-taking element may be porous, e.g. fibrous, e.g. in order to make it easy to impregnate with the analyte-taking liquid or the reagent.

By way of example, the analyte-taking element may be selected from the group constituted by: a cotton bud; a foam bud; a flocked bud; a felt tip; or a tip made of ceramic or sintered material; this list not being limiting.

The analyte-taking element may have adhesive or abrasive properties, e.g. for the purpose of taking a sample from the stratum corneum epidermis and/or elements present at the surface of the skin, a mucous membrane, the finger- or toe-nails, or the hair.

As mentioned above, the plug may comprise a liquid and/or a powder.

When the plug comprises a liquid, it may be selected from the group constituted by: mineral oils; fluorine-containing substances; and silicones, this list not being limiting.

Amongst powders that are suitable for constituting the plug, mention may be made by way of example of powders comprising organic or inorganic particles, which are solid or hollow, for example powders of microspheres of copolymers such as Expancel® (Nobel Industrie), Nylon® (in particular Orgasol®), waxes, silicas, or silicones, this list not being limiting.

The inside space of the tube may be defined at its end remote from the liquid or powder plug by a portion that can be broken off, that is removable, that can be perforated, or that is deformable.

The analyte-taking device may be arranged in such a manner that after the break-off end has been broken off, the user can measure out the quantity of liquid that flows out by handling the tube as a pipette, while closing the top end of the tube with an index finger, and with the tube optionally sloping to a greater or lesser extent, where appropriate.

In an embodiment of the invention, the tube may be reclosed after only a fraction of the liquid contained inside it has moved out. Such reclosing may be performed, for example, using the break-off end. This end may be configured, for example, in such a manner as to be capable of constituting a closure plug, the break-off end including a spike suitable for engaging in the tube or on the tube in order to close it.

Where appropriate, the device may include an element for holding the break-off portion to the analyte-taking device after it has been broken off.

The volume of liquid contained in the tube may lie, for example, in the range 0.01 millimeters (ml) to 5 ml,

or in the range 0.05 ml to 5 ml, or better in the range 0.05 ml to 1 ml. The volume of liquid may be suitable for a single use of the analyte-taking device.

The tube of the analyte-taking device may be made of a material that is transparent, in particular of a transparent plastics material, so as to enable the user to observe the level of the liquid inside the tube or to observe its color, for example.

The tube may comprise a multilayer structure, having at least one layer that constitutes a barrier against air, e.g. a layer of varnish that is impermeable to air, or to a solvent, or to ultraviolet (UV) radiation.

In another of its aspects, the invention also provides a kit for taking and analyzing an analyte, the kit comprising:

- at least one analyte-taking device comprising:
  - a tube;
  - a plug of liquid or powder inside the tube;
  - at least one analyte-taking liquid contained in an inside space of the tube defined at a first end by the liquid or powder plug; and
  - an analyte-taking element at one end of the tube, the analyte-taking element being separated from the analyte-taking liquid at least by the liquid or powder plug, the analyte-taking liquid being suitable for facilitating the taking of at least one analyte, the liquid or powder plug being suitable for being evacuated together with the analyte-taking liquid towards the analyte-taking element; and
- a reagent suitable, e.g. within the analyte-taking element, for producing an observable reaction in the presence of the analyte picked up by the analyte-taking element.

The kit may be presented in various ways.

For example, the kit may comprise a box including at least one compartment in which at least one analyte-taking device is housed.

In a variant, the kit may comprise at least one packaging bag containing at least one analyte-taking device.

By way of example, the reagent may be present on strips contained in the box.

In another of its aspects, the invention provides a method of detecting the presence and/or the concentration of at least one analyte, for example at the surface of tissue, in particular the skin of an individual, the method being characterized by the fact that it comprises the following steps:

· providing an analyte-taking device comprising a tube, a plug of a liquid or a powder inside a tube, at least one analyte-taking liquid contained in an inside space of the tube defined at a first end by the liquid or powder plug, and an analyte-taking element at one end of the tube, separated from the analyte-taking liquid by the liquid or powder plug;

· opening the tube so as to allow the analyte-taking liquid to leave the tube, the liquid or powder plug being suitable for being evacuated together with the analyte-taking liquid;

· taking at least one analyte with the analyte-taking element; and

· putting the analyte into contact with a reagent suitable for producing an observable reaction in the presence of said analyte or in the presence of a determined concentration of the analyte.

The invention also provides a method of detecting the presence and/or the concentration of at least one analyte, in particular an analyte present at the surface of the skin of an individual, the method being characterized by the fact that it comprises the following steps:

· providing an analyte-taking device comprising a tube having a break-off portion at one end and an analyte-taking element at its other end, a plug of liquid

or powder inside the tube, at least one reagent contained in an inside space of the tube defined at a first end by the plug of liquid or powder; and

· breaking the tube so as to allow the reagent to impregnate the analyte-taking element, the liquid or powder plug being suitable for being evacuated together with the reagent towards the analyte-taking element, and being suitable for revealing the presence of a determined analyte, optionally at a concentration that is greater than or less than a given threshold.

The invention can be better understood on reading the following detailed description of non-limiting embodiments of the invention, and on examining the accompanying drawings, in which:

· Figure 1 is a diagram showing a kit for taking and analyzing an analyte;

· Figures 2 to 4 show an analyte-taking device in isolation;

· Figures 5 to 7 show various ways in which the analyte-taking device can be used;

· Figure 8 shows a portion of another example of a kit for taking and analyzing an analyte;

· Figure 9 shows another example of an analyte-taking device;

· Figures 10 to 13 show variant embodiments of the analyte-taking element;

· Figures 14 to 16 show various embodiments of the breakable portion of the analyte-taking device;

· Figures 17 and 18 are diagrams showing analyte-taking devices that include two-phase or multi-phase reagents;

· Figure 19 is a diagrammatic and fragmentary view showing another example of an analyte-taking device;

· Figure 20 is a diagrammatic view of a receptacle suitable for receiving one or more analyte-taking devices; and

Figure 21 is a diagrammatic view of a support for an analyte-taking device.

Figure 1 is a diagram showing a kit for taking and analyzing an analyte comprising a box 10 comprising a base portion 11 and a lid 12 hinged to the base portion 11, which portion includes a plurality of compartments 13 housing analyte-taking devices 20, and a compartment 14 housing a plurality of strips 30 each comprising one or more zones 31 each impregnated with at least one reagent suitable for reacting with an analyte that can be taken by means of an analyte-taking device 20.

Figures 2 to 4 show an analyte-taking device 20 in isolation.

By way of example, this device may be a device similar to that described in US patent No. 5 702 035. Devices suitable for implementing the invention are put on the market by the California supplier Swabplus Inc.

Each device 20 comprises a tube 21 containing an analyte-taking liquid L, for example, the tube being made, in the assembly shown, by extruding a plastics material, and being provided at a closed end with a break-off portion 22. In the example described, this portion is covered by a cotton bud. The tube 21 is open at its other end remote from the break-off portion 22, being provided at this end with an analyte-taking element 23, for example.

In the example shown, the analyte-taking element 23 comprises a cotton bud in the manner of a cotton applicator.

The analyte-taking liquid L is contained in an inside space of the tube 21 situated between the break-off portion 22 and a plug 24 present in the tube 21 beside its open end. The plug 24 may be constituted by a liquid or by a powder.

The volume of analyte-taking liquid L may be suitable for a single use of the analyte-taking device, being determined as a function of the nature of the

liquid and of the analyte to be taken, and it may lie in the range, for example, 0.01 ml to 5 ml, and better in the range 0.05 ml to 1 ml. The outside diameter of the tube 21 may be less than 6 millimeters (mm), for example, or even less than about 3 mm. The inside diameter of the tube 21 may lie in the range about 0.5 mm to about 3 mm, for example.

When the plug 24 is formed by a liquid, the liquid of the liquid plug 24 may be constituted by any inert liquid that is compatible with packaging the liquid present in the tube 21, and in particular it may be constituted by a liquid that does not react with the analyte-taking liquid, that is capable of being evacuated easily from the tube 21 at the time of use, and that is also physiologically acceptable. The liquid plug 24 serves in particular to isolate the analyte-taking liquid L from air, preventing it from evaporating and preventing external contaminants from penetrating. The liquid of the liquid plug 24 may be constituted, for example, by a mineral oil or by a fluorine-containing substance, amongst other possibilities. In the example described, the liquid plug 24 is made of silicone.

The quantity of liquid forming the liquid plug 24 is small compared with the quantity of analyte-taking liquid L.

When the break-off portion 22 is broken off, air can penetrate into the tube 21 through its end remote from its open end, and the analyte-taking liquid L can flow under gravity inside the tube 21, thereby reaching the analyte-taking element 23, as shown in Figures 3 and 4, so as to be put into contact with tissue of an individual from which an analyte is to be taken, for example, in contact with the skin.

In the example described, the cotton bud covering the break-off portion 22 serves to hold it to the remainder of the tube 21, even after it has been broken off.

In order to use the analyte-taking device 20, the break-off portion of the tube is broken off, as shown in Figure 5 so that the analyte-taking liquid L flows into the analyte-taking element 23.

This element is then brought into contact with the skin, for example, which may be lightly massaged so that the analyte that is to be revealed and that is present at the surface of the skin becomes deposited on the analyte-taking element or diffuses into the analyte-taking liquid L.

Once the analyte has been taken, the analyte-taking element can be brought into contact with a reagent-impregnated zone 31, as shown in Figure 6. By way of example, the reagent may be configured so as to produce a colored reaction in the presence of a determined analyte as picked up by the analyte-taking element 23.

The analyte-taking liquid L may be water, for example, and in particular demineralized water, an aqueous solution, a water-alcohol solution, an alcohol solution, an oil solution, an oil, an organic solvent, being selected as a function of the analyte that is to be picked up, this list not being limiting.

The analyte whose presence on the surface of the skin is to be revealed may be, for example, an ion, in particular a carbonate, bicarbonate, calcium, or chlorine ion.

A strip 30 may comprise a plurality of zones 31, for example, each including reagents that react with different concentrations of a given analyte, so as to be capable of performing a quantitative measurement of the concentration of the analyte at the surface of the skin.

The liquid contained in the analyte-taking device may be an analyte-taking liquid as described with reference to Figures 1 to 6.

Alternatively, in the inside space situated between the plug 24 and the break-off portion 22, the tube 21 may contain a reagent in solution that is suitable for

producing a reaction, and in particular a colored reaction, within the analyte-taking element 23 when in the presence of a determined analyte picked up by the analyte-taking element.

Under such circumstances, and as shown in Figure 7, the analyte-taking element 23 may initially be impregnated with an analyte-taking liquid that is contained in a receptacle, e.g. it may be impregnated with demineralized water, and then the device 20 can be brought into contact with the skin in order to take any analyte that might be present thereon and that is suitable subsequently for reacting with the reagent contained in the tube 21, once the break-off portion of the device has been broken off.

It would not go beyond the ambit of the present invention for an analyte to be taken from the surface of the skin without previously impregnating the analyte-taking element with a liquid, particularly if the analyte in question is contained in sebum or in a body fluid.

Analyte-taking devices may be packaged in a box as shown in Figure 1, or they may be packaged in some other way without going beyond the ambit of the present invention, for example they may be packaged in the form of a string 32 of bags 33, as shown in Figure 8.

The analyte-taking element may alternatively be pre-impregnated with an analyte-taking liquid as shown in Figure 9. In which case, the liquid contained inside the tube 21 may contain a reagent suitable for revealing at least one analyte that might be present on the surface of the tissue of an individual.

The analyte-taking device 20 of Figure 9 may then be packaged in a hermetically sealed packaging bag 35 as shown in the figure.

The analyte-taking element can be provided in a variety of shapes, and in particular it can have an end that is rounded or tapering, for example it can be in the form of a pennon as shown in Figure 10.

By way of example, the analyte-taking element can be made of any porous material, e.g. fibrous material, and it may optionally be elastically compressible.

By way of example, and as shown in Figure 11, the analyte-taking element can be in the form of a foam bud 36.

The analyte-taking element can include flocking 37 on its surface, as shown in Figure 12. This figure also shows that the analyte-taking element can be curved in shape, with a portion extending along a longitudinal axis that does not coincide with the axis of the tube 21.

By way of example, the analyte-taking element can also be in the form of a bud 38 that is of tapering shape as shown in Figure 13. Such a bud can be made of a porous material, or, in a variant, of a material that is not porous but that includes at least one internal channel or groove that enables the liquid contained in the tube 21 to be flow towards the distal end.

The analyte-taking element can be made in such a manner as to be capable of exerting abrasive action, e.g. on the skin, in order to take cells.

The analyte-taking element can be made of ceramic or of sintered material, for example.

It is also possible for the analyte-taking element to be made by giving the tube a chamfered-shape, for example, thus enabling analytes to be taken by scratching.

The analyte-taking element may also present adhesive properties.

Figures 14 to 16 show other embodiments of the break-off portion of the applicator.

Figure 14 shows that the break-off portion can be connected to the remainder of the tube via a preferred breakage zone 27, e.g. implemented in the form of a filling in the wall of the tube or a notch at this level.

The break-off portion may be made in various other manners without going beyond the ambit of the present invention.

In particular, as shown in Figure 15, the applicator can be configured in such a manner that the break-off portion 22 is capable of being completely separated from the tube 21 after manually applying a breaking movement by holding the tube 21 in one hand and the break-off portion 22 between two fingers of the other hand.

The applicator can alternatively be configured in such a manner that, after use, the break-off portion 22 remains connected to the tube 21 via a bridge of material 50, as shown in Figure 16.

The end of the tube can be made in other ways, for example in one of the ways shown in Figures 3 to 8 of US patent No. 3 958 571.

When the break-off end is capable of being completely detached from the tube, that can make it easier to use the analyte-taking device as though it were a pipette, for example, with the user being capable of closing the top end of the analyte-taking element with a finger in order to dispense the liquid into the analyte-taking element in controlled manner, e.g. drop by drop.

Figure 17 shows a tube including two liquid reagents P_1 and P_2 that are present in the form of two phases each occupying a fraction of the length of the tube.

The two reagents P_1 and P_2 are in contact with each other via an interface 60.

One of the reagents may also be present in the form of at least one globule within the other phase, for example in the form of a plurality of globules 61 as shown in Figure 18. This can make it possible, for example, to measure out the liquid using the tube as a pipette, or to improve the appearance of the applicator.

A plurality of different liquids can also be dispersed in the form of a plurality of globules in a single phase. The various globules can thus correspond

to reagents of different colors and/or containing reagents at different concentrations and/or of different kinds.

When contained in the tube, it is also possible for the reagent P_2 to be solid, e.g. being constituted by a powder that is soluble in the liquid P_1, the substances P_1 and P_2 being separated from each other prior to use by a plug. The volume of the substance P_2 may be small enough to ensure that the substance P_2 can be dissolved easily in use.

The number of substances present in the analyte-taking device may be greater than two, without thereby going beyond the ambit of the present invention.

Figure 19 shows the top end of a tube that contains three internal channels 56 by way of example, each containing a respective liquid and an associated plug, the tube being closeable at this end prior to use by a removable capsule 57 which can be stuck or heat-sealed on the tube, for example.

Figure 20 shows a receptacle suitable for receiving an analyte-taking device.

By way of example, such a receptacle may comprise a stand 50 supporting a body 55 whose top end is configured to enable a closure cap 51 to be fixed in place to close the receptacle in substantially leaktight manner, a support element 52 being disposed inside the body and having at least one orifice 53 enabling an analyte-taking device 20 to be engaged therein.

Thus, if so desired, after taking an analyte, the user may place the analyte-taking device in the receptacle. The presence of the cap 51 makes it possible to avoid the analyte-taking element drying out, for example.

It is also possible to use an analyte-taking device with a support 70 of the kind shown in Figure 21, enabling the analyte-taking device to be held with its analyte-taking element visible, which support may

include, for example, means 71 enabling the break-off end to be broken off when the analyte-taking device is put into place in the support 70. By way of example, these means 71 comprise a window giving access to the break-off end, or an element that is movable relative to the support and which applies lateral thrust on the break-off end when actuated. The tube need not have a break-off end but may merely have an end that is closed, with the support 70 being fitted with a blade or a spike, for example, serving to cut or pierce the tube so as to allow air to penetrate into the inside, and the liquid and the plug to be evacuated when the analyte-taking device is used.

Naturally, the invention is not limited to the embodiments described above.

A device of the invention can have numerous applications.

In addition to the applications described above, the invention makes it possible amongst other things to evaluate the activity of acid phosphatase, which can be representative of the extent to which the skin has been harmed by detergents, to evaluate catalase, or to evaluate barrier function deficiency or the buffering ability of the skin.

The end of the tube 21 opposite from the end through which the substance leaves may, for example, be closed other than by means of a portion suitable for being broken off manually, for example it may be closed by means of a plug or a piston.

The tube 21 may be made with an enlarged portion, e.g. in order to enable pressure to be exerted on the liquid so as to cause it to leave the tube.

The term "tube" is used to cover any body that is preferably generally elongate and of optionally constant section that presents at least one internal channel capable of containing a liquid, and such a tube may present a longitudinal axis that is rectilinear or

otherwise. The invention is not limited to a tube of circular outside section, nor is it limited to a tube made in accordance with the teaching of US patent No. 5 702 035.

Throughout the description, including in the claims, the term "comprising a" should be understood as being synonymous with "comprising at least one", unless specified to the contrary.